IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: SOLOMON2B.2

In re Application of:	)	Conf. No.: 9533
Beka SOLOMON et al.	)	Art Unit: 1649
Appln. No.: 10/749,522	)	Examiner: G. Emch
Filed: January 2, 2004	)	Washington, D.C.
For: AGENTS AND COMPOSITIONS AND METHODS UTILIZING SAME USEFUL IN …	)	April 13, 2009

RESPONSE

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Randolph Building, Mail Stop Amendments
401 Dulany Street
Alexandria, VA 22314

Sir:

The present communication is responsive to the Official Action of November 13, 2008. Claims 1-11 and 25-34 presently appear in this case. Claims 1-6 have been withdrawn from consideration. No claims have been allowed. The Official Action of November 13, 2008, and the references relied upon therein have now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to filamentous bacteriophage consisting of filamentous bacteriophage that displays an antibody or an antigen-binding fragment thereof. The antibody or fragment binds to an epitope of β-amyloid so as

to inhibit aggregation or cause disaggregation of β-amyloid aggregate in the subject. The filamentous bacteriophage may be part of a composition with a carrier, and, in a preferred embodiment, as an active ingredient of a pharmaceutical composition with a pharmaceutically acceptable carrier.

It is noted that the examiner has considered applicant's replies filed on September 12, 2007, and October 15, 2007, with respect to the rejections of claims 7-11 and 25-34 under 35 USC 103(a) and have considered them to be persuasive. Therefore, these rejections have been withdrawn.

In a new rejection, claims 7-11 and 25-35 have been rejected under 35 USC 103(a) as being unpatentable over Solomon and Hanan, both as evidenced by Frenkel, and both in view of Ruoslahti and Prusiner. The examiner states that Solomon, Hanan and Frenkel disclose monoclonal antibodies that bind to β-amyloid so as to inhibit aggregation of β-amyloid in the subject and/or to cause disaggregation of a β-amyloid aggregate in a subject. The examiner recognizes that neither Solomon nor Hanan teach compositions comprising filamentous bacteriophage which displays an antibody or epitope binding fragment thereof. The examiner states that Ruoslahti teaches an *in vivo* panning method that comprises screening of a phage peptide display library in mice and identifying specific peptides that selectively home to brain or kidney. The phage peptide display library may display antibodies or an antigen binding fragment

thereof. The examiner thus considers that Ruoslahti teaches that an antibody or epitope binding fragment thereof can be displayed on a bacteriophage for *in vivo* administration. Prusiner is cited for the dependent claim that specifies that the antibody is on coat glycoprotein VIII. The examiner states that developing alternative antibody compositions would be desirable and that it would have been obvious "to improve the antibodies or epitope binding fragments as disclosed by Ruoslahti et al. and Prusiner et al. to yield predictable results." The examiner states that Ruoslahti explicitly teaches displaying an antibody on a bacteriophage for *in vivo* use "i.e., diagnostic use." Without further explanation, the examiner states that Ruoslahti explicitly teaches an advantage of displaying an antibody or epitope binding fragment thereof on a bacteriophage and that the composition of Ruoslahti can be used "for diagnostic usage to identify molecules that home to the brain." This rejection is respectfully traversed.

The bottom line of the present invention is the examiner's assertion that one of ordinary in the art at the time the invention was made would have found it obvious to display the specific antibody of Solomon and Hanan on a filamentous phage. The examiner states that the motivation to do so would have been the disclosure of Ruoslahti that such an antibody-displayed phage could be used for a diagnostic use *in vivo*. The examiner states that it would have been obvious "to

improve the antibodies or epitope binding fragments as disclosed by Ruoslahti et al. and Prusiner et al. to yield predictable results" (last line of page 7 of the Official Action of November 13, 2008). But the examiner nowhere explains where in the disclosures of Ruoslahti or Prusiner is there any suggestion that antibodies can be improved by displaying them on a phage.

The examiner states that at page 9 that the advantage of displaying an antibody on a bacteriophage is for a diagnostic use. However, this argument of the examiner fails because Ruoslahti teaches absolutely no diagnostic use for a filamentous phage displaying an antibody. Indeed, the word "diagnostic" (or any cognate thereof) appears only twice in the entire Ruoslahti patent. One is at column 12, line 52, and the other is at column 13, line 47. In both cases, Ruoslahti is referring to the molecule that is obtained using the phage display library as a tool. The "molecule" is that antibody which has been identified using the phage display library of Ruoslahti, not any phage displayed antibody. Note the definition of "molecule" in Ruoslahti at the paragraph beginning at page 3, line 46. This definition does not include the presence of phage. The phage is used to identify the molecule. Once the molecule is identified, it is the molecule that is used as the organ homing molecule, not the phage displaying that molecule. Note, for example, in Example II,

section C, beginning at column 18, line 60. Once the phage display library is used to identify the organ homing molecule, in that case, a peptide, the peptide is synthesized and used in further tests. There is absolutely nothing in Ruoslahti that the examiner can point to which suggests use of a phage displayed antibody other than as part of a screening process.

The examiner states that at page 10 that Ruoslahti teaches a composition "comprising an antibody or epitope binding fragment displayed on a bacteriophage for diagnostic use to identify molecules that home to the brain." The examiner is correct that Ruoslahti uses the bacteriophage to identify molecules that home to the brain; however, the examiner is totally wrong in stating that this is a "diagnostic use." This is nothing more than a screen. The organ homing antibodies that are found using the process are then synthesized or otherwise produced and then used *per se* for diagnostic purposes. **There is nothing in Ruoslahti suggesting that a phage-displayed antibody can be used for diagnostic purposes.** The libraries of phage-displayed antibodies or other peptides are only used for "*in vivo* panning." After administration, the animals are sacrificed or otherwise biopsied to get a portion of the organ of interest and see which phage bound to the organ. The phage containing a peptide that binds to the organ is then selected from out of the entire library and the peptide or antibody that is displayed thereon

is identified. The organ homing molecule that is so identified can then be used for diagnostic or therapeutic purposes, as is disclosed for example beginning at column 12, line 24.

There is no disclosure anywhere in Ruoslahti about the diagnostic or therapeutic use of a phage displaying an organ homing molecule or the use of such a phage displaying a specific organ homing molecule as a delivery system.

What then is the motivation to display the molecule of Solomon and Hanan, which molecule has already been identified, on a phage and then administer it for any purpose? The examiner states without explaining that there is some kind of advantage in displaying an antibody on a bacteriophage for *in vivo* use. But the only advantage taught by Ruoslahti is that entire libraries of phage can be administered in order to select for the molecules displayed thereon that bind to a particular organ. That is not a diagnostic use and that is not a therapeutic use. That is a use to screen for antibodies (i.e., to find useful antibodies). **There is absolutely no reason whatsoever why one of ordinary skill in the art would use phage display technology with an antibody that has already been identified and selected.** The examiner is challenged to explain any possible motivation provided by the prior art or by common sense for taking an antibody that has already been selected and putting it on a filamentary phage. Ruoslahti provides none.

It is conceded that one of ordinary skill in the art would know how to put such an antibody on the pVIII coat protein of a phage; however, this is insufficient to establish obviousness. There must be some reason for one of ordinary skill in the art to do so. Ruoslahti provides absolutely no reason to put the specific antibody of Solomon and Hanan onto a filamentous phage. Neither does any other reference of record or "common sense."

Accordingly, it can be seen that the arguments previously provided, which the examiner has conceded were persuasive, apply equally to the present rejection where Ruoslahti was substituted for Pasqualini. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

It is submitted that all of the claims now present in case clearly define over the references of record and fully comply with 35 U.S.C. 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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